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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,220	01/31/2002	Burkhard Schulz	DEBE 1PCT SEQ/dln	1762

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 07/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,220	SCHULZ, BURKHARD	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-26* is/are pending in the application.

4a) Of the above claim(s) *16,21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,15,17-20 and 23-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 August 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/22/2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 14-26 are pending.

2. Applicant's election with traverse of Group II, claims 14-15, 17-20 and 23-26 including SEQ ID NO:2, in the reply filed on 6/14/2004 is acknowledged. The traversal is on the ground(s) that Applicants contend that the Xu et al (1998, The Plant Journal 15:511-519) reference only teaches an amino acid sequence. Applicants have presented a pairwise sequence alignment of the FKBP-12 amino acid sequence disclosed in Xu et al and the instant amino acid sequence of SEQ ID NO:3. Applicants contend that the proteins exhibit 33% identity at the amino acid level and do not possess a common fragment, as indicated by the Office. Based on this result, Applicants contend that the restriction requirement in which Groups I-IV do not possess a common special technical feature is unfounded (paragraph bridging pages 1 and 2 of Applicants response).

This is not found persuasive because the claims are drawn to a fragment of SEQ ID NO:1, and the Office interprets a fragment as comprising at least one base pair. Therefore, the nucleic acid of Xu et al would have at least one base pair in common with Applicant's SEQ ID NO:1. The Office submits Peattie et al (June 1998, U.S. Patent 5,763,590) as teaching a fragment of Applicant's SEQ ID NO:2 (See item 11, below) and as such, there is no special technical feature that links or is shared by Applicant's claims.

Claims 16 and 21-22 are withdrawn from consideration for reading on non-elected inventions.

3. Claims 14-15, 17-20 and 23-26, including SEQ ID NO:2 are examined in the present office action.

Specification

4. On page 18, line 10, the specification is objected to for reciting "von".

On pages 9, line 15 and page 14, line 24, "ethylene" is misspelled.

The Specification is objected to because the drawings are not referred to properly. If the drawings show Figures 1A, 1B, and 1C, then the Brief Description of the Drawings should recite "Figures 1A-1C", instead of "Figure 1". Correction is requested.

Drawings

5. The recitation "Figure" is misspelled in the drawings.

Information Disclosure Statement

6. The Foreign Patent Documents listed on form 1449 have not been considered as they were not provided by the Applicant. As stated in the MPEP § 1.98 (a) Any information disclosure statement filed under § 1.97 shall include: (1) A list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) A legible copy of:

(i) Each foreign patent;

(ii) Each publication or that portion which caused it to be listed;

In addition, each publication listed in an information disclosure statement must be identified by publisher, author (if any), title, relevant pages of the publication, date, and place of publication. (See 37 CFR 1.98).

Claim Objections

7. Claims 14 and 15 are objected to for reading on non-elected sequences.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 14-15, 17-20, and 23-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a fragment or derivative of SEQ ID NO:2, or a nucleic acid sequence that hybridizes with SEQ ID NO:2, or wherein the hybridization is under stringent conditions, a vector, method and transgenic plant comprising said sequence.

Applicant isolated the invention from an *Arabidopsis thaliana* line transformed with T-DNA, in which a 200 bp long DNA sequence of the TWISTED DWARF (TWD) gene flanking the T-DNA insertion was isolated through plasmid rescue. Using the isolated DNA as a probe, the CD4-7 PRI-2 cDNA library was screened and a clone was isolated (page 18, line 13-24). Applicant discloses the cDNA clone as SEQ ID NO:2 (page 8, lines 23-24).

The Applicant does not identify essential regions of TWD protein encoded by SEQ ID NO:2, nor does Applicant describe any fragments or derivative sequences thereof, or any

sequences that hybridize to SEQ ID NO:2 that encodes a functional TWD protein. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicants fail to describe a representative number of polynucleotide sequences encoding a TWD protein falling within the scope of the claimed genus of polynucleotides that are fragments or derivatives of SEQ ID NO:2 or nucleic acids which hybridize to SEQ ID NO:2. Applicants only describe a single cDNA sequence of SEQ ID NO:2. Furthermore, Applicant fails to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the TWD protein, it remains unclear what features identify an Arabidopsis TWD protein. Since the genus of TWD proteins has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Enablement

9. Claims 14-15, 17-20, and 23-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to a fragment or derivative of SEQ ID NO:2, or a nucleic acid sequence that hybridizes with SEQ ID NO:2, or wherein the hybridization is under stringent conditions, a vector, method for the production of plants and transgenic plant, plant cell or seeds comprising said sequence, wherein the method also comprises homologous recombination.

Applicant isolated the invention from an *Arabidopsis thaliana* line transformed with T-DNA, in which a 200 bp long DNA sequence of the TWISTED DWARF (TWD) gene flanking the T-DNA insertion was isolated through plasmid rescue. Using the isolated DNA as a probe, the CD4-7 PRI-2 cDNA library was screened and a clone was isolated (page 18, line 13-24).

Applicant discloses the cDNA clone as SEQ ID NO:2 (page 8, lines 23-24). Applicants disclose that plants mutant for the TWD gene were complemented by transformation using the open reading frame of the TWD sequence (page 19-20, Example 3).

Applicant has not reduced to practice the invention. The specification fails to provide guidance for one of skill in the art how to make and/or use the claimed invention. Applicant has not transformed a wild-type plant with any of the claimed sequences to produce a plant with any of the desired phenotypes as listed on page 9, lines 7-20. Applicant has only taught that SEQ ID NO:2 transformed into a *twd* mutant plant will complement the mutation. Applicant has not taught how one skilled in the art can use the claimed sequence to generate any of the disclosed phenotypes as listed on page 9, lines 7-20, without having to do additional undue experimentation in order to achieve the desired results. In addition, Applicant has not taught how one skilled in the art would use a plant transformed with any of the claimed sequences.

The state-of-the-art teaches that homologous recombination in plants is unpredictable. Babiychuk et al (1997 Proc. Natl. Acad. Sci. 94:12722-12727) teach that homologous recombination in plants is very low (page 12722, left column) and that it is doubtful that homologous recombination will be practical in plants (page 12724, left column, 1st paragraph).

Applicants have not disclosed how one makes or isolates any of the sequences that are encompassed by Applicants' broad claims. Applicants have not taught which regions of the respective polynucleotides can be used to amplify any of said polynucleotides or which regions can be used as a probe to isolate any of said polynucleotide sequences.

The state-of-the-art is such that one of skill in the art cannot predict which nucleic acids that are fragments or nucleic acid sequences derived from SEQ ID NO:2 will encode a protein

with the same activity as a protein encoded by SEQ ID NO:2. The prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex, and the positions within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of maintaining function are limited (Bowie et al, Science 247:1306-1310, 1990, see especially page 1306). Proteins may be sensitive to alterations in even a single amino acid in a sequence. For example, the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain (McConnell et al, Nature 411 (6838):709-713, 2001, see especially page 710, left column, 2nd paragraph).

Applicants claims are drawn to nucleic acid sequences that hybridize to SEQ ID NO:2, but the state-of-the-art teaches isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^0C (page 859, left column, 2nd paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2). In the present

example, the isolated fragment of Frourgoux-Nicol et al exhibits less than 50% sequence identity with the probe to which the fragment hybridized.

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of SEQ ID NO:2 as probes or by designing primers to undisclosed regions of SEQ ID NO:2 and isolating or amplifying fragments or derivatives thereof, subcloning the fragments or derivatives thereof, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when over-expressed produce a plant with an agronomically useful phenotype.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 14 and 15 are directed to non-statutory subject matter. This rejection is made because the claims are drawn to "A nucleic acid sequence" which does not indicate that the "hand of man" was involved in the invention. Amending the claim to recite "isolated" will obviate the rejection.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 14-15 and 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Peattie et al (June, 1998, U.S. Patent Number 5,763,590).

The claims are drawn to a nucleic acid sequence that is a fragment or a derivative of SEQ ID NO:2 or a nucleic acid sequence that hybridizes with SEQ ID NO:2, wherein the sequence hybridizes under stringent conditions and the nucleic acid sequence having the biological activity of a nucleic acid sequence of SEQ ID NO:2, and a vector comprising said nucleic acid sequence and further comprising one or more regulatory elements.

Peattie et al disclose a nucleic acid sequence that encodes a 52 kD human FK506 binding protein (FKBP52) and exhibits 4.5% sequence identity with Applicant's SEQ ID NO:2 (See attached sequence search result). Applicant's SEQ ID NO:2 also encodes a FK506 binding protein (*ibid*). The Office interprets the recitations "fragment" and "derivative" to read on one base pair and the Office interprets "stringent conditions" to mean low stringent conditions which means that the sequence of Peattie et al would hybridize with Applicant's SEQ ID NO:2 given the 47.5% local sequence identity (*ibid*) and the nucleic acid sequence would have the same biological activity as Applicant's nucleic acid sequence. The Office interprets "biological activity" of a nucleic acid sequence to mean that the nucleic acid sequence encodes a protein. The sequence of Peattie et al is included in a vector and comprises regulatory elements (columns 12-14, Examples 4, and 6) and as such, Peattie et al anticipate the claimed invention.

12. Claims 14-15, 17-20, and 24-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Holt (February, 1999, U.S. Patent Number 5,866,791).

The claims are drawn to a nucleic acid sequence that is a fragment or a derivative of SEQ ID NO:2 or a nucleic acid sequence that hybridizes with SEQ ID NO:2, wherein the sequence hybridizes under stringent conditions and the nucleic acid sequence having the biological activity of a nucleic acid sequence of SEQ ID NO:2, and a vector comprising said nucleic acid sequence and further comprising one or more regulatory elements, a method for the production of plants comprising said nucleic acid sequence operably linked to one or more regulatory elements, and a transgenic plant and seeds comprising said nucleic acid sequence.

Holt discloses a DNA sequence that comprises a fragment or derivative of Applicant's SEQ ID NO:2 (Claim 1 of Holt). The Office interprets the recitations "fragment" and "derivative" to read on one base pair and the Office interprets "biological activity" of a nucleic acid sequence to mean that the nucleic acid sequence encodes a protein. Holt discloses a recombinant DNA comprising said sequence operably linked to transcription initiation sequence which the Office interprets as a regulatory element (Claim 2 of Holt). It would be inherent that the sequence of Holt with accompanying transcription initiation sequence would be included in a vector. Holt teaches a plant and seed transformed with said sequence and accompanying transcription initiation sequence and the plant of Holt inherently teach a method for the production of plants comprising said sequence and accompanying transcription initiation sequence, and as such, Holt anticipates the claimed invention (Claims 5, 7, 8 of Holt).

13. Claim 23 is deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest a method for the production of plants comprising transforming a plant with SEQ ID NO:2 or claimed sequence variants thereof, wherein the nucleic acid sequence is integrated into the endogenous gene in the plant genome via homologous recombination.

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
July 19, 2004